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(FILE 'HOME' ENTERED AT 11:25:15 ON 26 FEB 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:25:28 ON 26 FEB 2002
E OSTEOSCREEN/PA, CS
L1 13 S E3-E12
E OESTEOSCREEN/PA, CS
E MUNDY G/AU
L2 256 S E3, E6, E8-E10
E GARRETT R/AU
E GARRETT R/AU
L3 55 S E3
E GARRETT ROSS/AU
L4 7 S E3, E4
E ROSSINI G/AU
L5 80 S E3-E16
E GARRETT I/AU
L6 53 S E3-E7
L7 422 S L1-L6
L8 4 S L7 AND ?PROTEASOM?

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FILE 'REGISTRY' ENTERED AT 11:29:20 ON 26 FEB 2002
L9 1 S 140879-24-9

FILE 'HCAPLUS' ENTERED AT 11:30:15 ON 26 FEB 2002
L10 2944 S L9
L11 4723 S PROTEASOME OR PROSOME OR (26S OR 26 S) (L) PROTEASE OR IMMUNOPR
L12 21 S TRICORN () (PROTEASE OR PROTEINASE)
L13 4 S L7 AND L10-L12
L14 4 S L8, L13
L15 11143 S NF (L) KAPPA (L) B
L16 8204 S NUCLEAR (L) FACTOR (L) KAPPA (L) B
L17 4 S L7 AND L15, L16
L18 5 S L14, L17
L19 21 S EPOXOMICIN# OR EPOXYOMYCIN#
L20 41 S PS341 OR PS 341
L21 46 S NLVS
E ALDEHYDE/CT
L22 166 S E15(L) (PEPTIDE OR PEPTIDYL)
L23 1055 S E15+NT(L) (PEPTIDE OR PEPTIDYL)

FILE 'REGISTRY' ENTERED AT 11:40:11 ON 26 FEB 2002
L24 1 S 6493-05-6
L25 1 S 133343-34-7
L26 7 S LACTACYSTIN
L27 3 S L26 AND C15H24N2O7S
L28 19 S C15H24N2O7S/MF
L29 6 S L28 AND NC4/ES AND 1/NR
L30 3 S L29 NOT (T/ELS OR GLYCINE)
L31 1 S 134381-21-8
L32 9 S C28H50N4O7/MF
L33 3 S L32 AND OC2/ES AND 1/NR
L34 2 S L33 NOT T/ELS
L35 1 S 179324-69-7
L36 1 S C19H25BN4O4/MF AND NC2NC2/ES AND 46.150.18/RID AND 2/NR
L37 1 S 158442-41-2
L38 41 S C32H50N4O8/MF
L39 14 S L38 AND 4/SQL
L40 3 S L39 AND 46.150.18/RID AND 1/NR
L41 1 S 193482-49-4
L42 3 S C28H43IN4O8S/MF

L43 2 S L42 NOT 125I
L44 10 S L24,L25,L30,L31,L34,L35,L36,L37,L41,L43
SEL RN
L45 16 S E1-E10/CRN
L46 3 S L45 NOT MXS/CI
L47 13 S L44,L46
L48 13 S L45 NOT L47

FILE 'HCAPLUS' ENTERED AT 11:49:48 ON 26 FEB 2002
L49 1978 S L47
L50 5 S L48
L51 548 S LACTACYSTIN#
L52 2396 S PTX
L53 4729 S L19-L22,L49-L52

FILE 'REGISTRY' ENTERED AT 11:50:44 ON 26 FEB 2002
L54 STR
L55 3 S L54
L56 STR L54
L57 1 S L56
SAV L44 GITOMER1/A TEMP
SAV L45 GITOMER2/A TEMP
DEL GITOMER1/A
DEL GITOMER2/A
SAV TEMP L47 GITOMER1/A
SAV TEMP L48 GITOMER2/A
SAV L56 GITOMER3/Q

FILE 'HCAPLUS' ENTERED AT 11:57:11 ON 26 FEB 2002
L58 3 S L7 AND L53
L59 5 S L18,L58

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FILE COVERS 1907 - 26 Feb 2002 VOL 136 ISS 9
FILE LAST UPDATED: 25 Feb 2002 (20020225/ED)

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The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches

and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

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L59	ANSWER 1 OF 5	HCAPLUS	COPYRIGHT 2002 ACS	
AN	2001:300537	HCAPLUS		
DN	134:331618			
TI	Inhibitors of proteasomal activity for stimulating bone and hair growth			
IN	Mundy, Gregory R.; Garrett, Ross I.; Rossini, G.			
PA	Osteoscreen, Inc., USA			
SO	PCT Int. Appl., 57 pp.			
	CODEN: PIXXD2			
DT	Patent			
LA	English			
IC	ICM A61K038-06 ICS A61K038-07; A61K038-13; A61K031-165; A61K031-365; A61K031-4015; A61K031-522; A61P019-00; A61P043-00			
CC	63-6 (Pharmaceuticals) Section cross-reference(s): 1, 62			
FAN.CNT 1				
	PATENT NO.	KIND	DATE	APPLICATION NO.
PI	WO 2001028579	A2	20010426	WO 2000-US41360
	WO 2001028579	A3	20010920	20001020
	W: AU, CA, JP RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
PRAI	US 1999-421545	A	19991020	
	US 2000-558973	A	20000425	
AB	Compds. that inhibit the activity of NF-.kappa. B or inhibit the activity of the proteasome or both promote bone formation and hair growth and are thus useful in treating osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation; they also stimulate the prodn. of hair follicles and are thus useful in stimulating hair growth, including hair d., in subject where this is desirable. N-carbobenzoyl-Ile-Glu-(OtBu)Ala-Leu-CHO (PSI) in 50% propylene glycol, 10% DMSO, and 40% water was injected daily for 5 days (1mg/kg body wt./day) into the s.c. tissue of mice and the tissue was examed. histol. 16 days later. The no. of hair follicles increased and the downward extension of these hair follicles into the dermal tissue was noted, which are hallmarks of anagen. There was an obvious increase in size of the follicle diam. and the root sheath diam.			
ST	proteasome inhibitor hair bone growth stimulant			
IT	Transcription factors			
	RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(I.kappa.B (inhibitor of NF-.kappa.B); inhibitors of proteasomal activity for stimulating bone and hair growth)			
IT	Periodontium			
	Tooth (disease; inhibitors of proteasomal activity for stimulating bone and hair growth)			
IT	Hair (follicle; inhibitors of proteasomal activity for stimulating bone and hair growth)			

IT Bone, disease
(fracture; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Bone
Hair preparations
(growth stimulants; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Dental materials and appliances
(implants; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Bone formation
(inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Bone morphogenetic proteins
Estrogens
Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Bone, disease
(metastatic and osteolytic; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenins; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Surgery
(post-plastic; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Hyperparathyroidism
(secondary; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Phosphoproteins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statins; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Joint, anatomical
(surgery of; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Osteoporosis
(therapeutic agents; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonate; inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT 67-99-2, Gliotoxin 404-86-4, Capsaicin 6493-05-6, PTX
9035-81-8, Trypsin inhibitor 25769-03-3, PDTC 59865-13-3, Cyclosporin a 65240-86-0, PPM 18 79902-63-9, Simvastatin 110044-82-1
110115-07-6 133343-34-7, Lactacystin 133407-82-6, MG 132 133407-86-0, MG 115 134381-21-8, Epoxomicin 158442-41-2D, PSI, epoxides 179324-22-2, MG 262
179324-69-7, PS 341 336099-20-8
336099-21-9 336608-38-9, Bay 11-7082
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT 140879-24-9, Proteasome

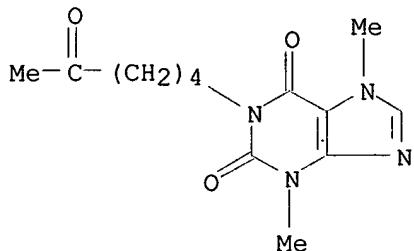
RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; inhibitors of proteasomal activity for
 stimulating bone and hair growth)

IT 6493-05-6, PTX 133343-34-7,
 Lactacystin 134381-21-8, Epoxomicin
 158442-41-2D, PSI, epoxides 179324-69-7, PS
 341

RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibitors of proteasomal activity for stimulating bone and
 hair growth)

RN 6493-05-6 HCPLUS

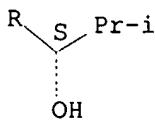
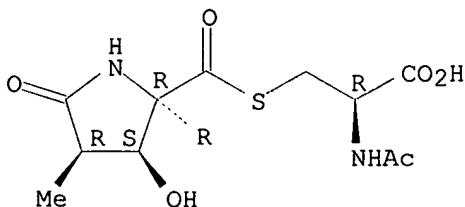
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA
 INDEX NAME)



RN 133343-34-7 HCPLUS

CN L-Cysteine, N-acetyl-, (2R,3S,4R)-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA
 INDEX NAME)

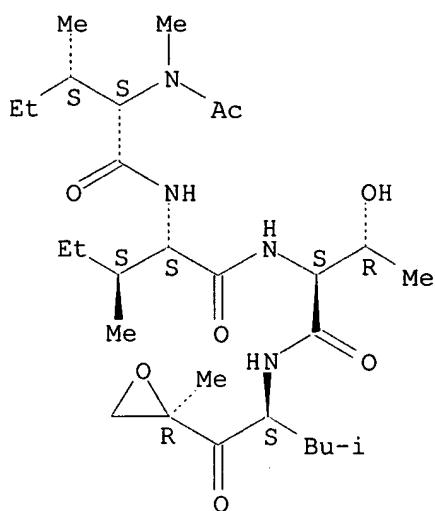
Absolute stereochemistry. Rotation (+).



RN 134381-21-8 HCPLUS

CN L-Threoninamide, N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[(2R)-2-methyloxiranyl]carbonyl]butyl]- (9CI) (CA INDEX NAME)

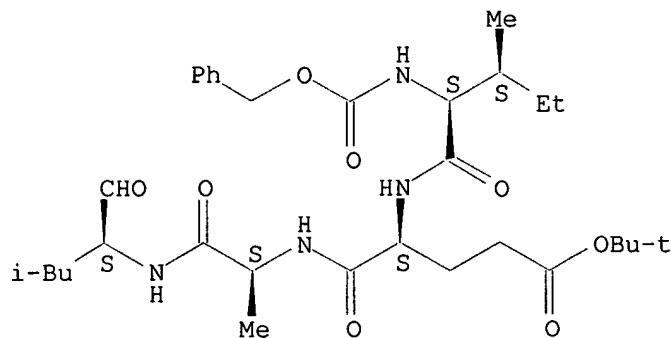
Absolute stereochemistry.



RN 158442-41-2 HCAPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

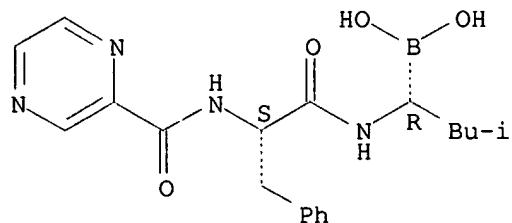
Absolute stereochemistry.



RN 179324-69-7 HCAPLUS

CN Boronic acid, [(1R)-3-methyl-1-[(2S)-1-oxo-3-phenyl-2-[(pyrazinylcarbonyl)amino]propyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 140879-24-9, Proteasome

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; inhibitors of proteasomal activity for
stimulating bone and hair growth)

RN 140879-24-9 HCAPLUS

CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L59 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:240712 HCAPLUS

DN 135:18367

TI Therapeutic efficacy of a soluble receptor activator of **nuclear factor .kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in a model of humoral hypercalcemia of malignancy

AU Oyajobi, Babatunde O.; Anderson, Dirk M.; Traianedes, Kathy; Williams, Paul J.; Yoneda, Toshiyuki; Mundy, Gregory R.

CS Division of Endocrinology, Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX, 78229, USA

SO Cancer Res. (2001), 61(6), 2572-2578
CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

CC 15-5 (Immunochemistry)

AB Receptor activator of **NF-.kappa.B** (RANK) is a membrane-bound tumor necrosis factor receptor homolog that mediates signals obligatory for osteoclastogenesis as well as osteoclast activation and survival in vivo. The present study was undertaken to evaluate the efficacy of a sol. murine RANK-human Ig fusion protein (muRANK.Fc) as a bone resorption inhibitor in vitro and in vivo. The in vitro studies demonstrated the ability of muRANK.Fc to inhibit human parathyroid hormone-related protein (PTHrP)-induced resorption in fetal rat long bone cultures. Short-term administration of muRANK.Fc to normal growing mice resulted in a complete disappearance of osteoclasts from metaphyses of long bones assocd. with a pronounced increase in calcified trabeculae and bone radiodensity. In a model of humoral hypercalcemia of malignancy in which PTHrP secreted by s.c. xenografts of human lung cancer in nude mice induces extensive osteolysis and severe hypercalcemia, daily administration of muRANK.Fc from time of tumor implantation profoundly inhibited osteoclastic bone resorption and prevented hypercalcemia. MuRANK.Fc had no effect on tumor prodn. of PTHrP, because there was no difference between circulating human PTHrP levels in muRANK.Fc-treated and vehicle-treated tumor-bearing mice. Moreover, even when treatment was initiated after hypercalcemia was established, muRANK.Fc attenuated further increases in blood ionized calcium. These data demonstrate the potent anti-resorptive effects of muRANK.Fc in vivo as well as highlight the potential utility of disrupting RANK signaling as a novel therapeutic approach in humoral hypercalcemia of malignancy and possibly multiple myeloma and skeletal metastases assocd. with osteolysis.

ST RANK IgG Fc fusion protein bone resorption hypercalcemia malignancy

IT Immunoglobulins

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(G, Fc, fusion protein contg.; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT Proteins, specific or class

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(RANK, sol., fusion protein contg.; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT Neoplasm

(humoral hypercalcemia of malignancy; therapeutic efficacy of sol.

receptor activator of NF-.kappa.B-IgG Fc
 fusion protein in suppressing bone resorption and hypercalcemia in
 humoral hypercalcemia of malignancy model)
 IT Osteoclast
 (inhibition; therapeutic efficacy of sol. receptor activator of
 NF-.kappa.B-IgG Fc fusion protein in
 suppressing bone resorption and hypercalcemia in humoral hypercalcemia
 of malignancy model)
 IT Bone
 (resorption, inhibitors; therapeutic efficacy of sol. receptor
 activator of NF-.kappa.B-IgG Fc fusion
 protein in suppressing bone resorption and hypercalcemia in humoral
 hypercalcemia of malignancy model)
 IT Signal transduction, biological
 (therapeutic efficacy of sol. receptor activator of NF-
 .kappa.B-IgG Fc fusion protein in suppressing bone
 resorption and hypercalcemia in humoral hypercalcemia of malignancy
 model)
 IT 7440-70-2, Calcium, biological studies
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (hypercalcemia; therapeutic efficacy of sol. receptor activator of
 NF-.kappa.B-IgG Fc fusion protein in
 suppressing bone resorption and hypercalcemia in humoral hypercalcemia
 of malignancy model)

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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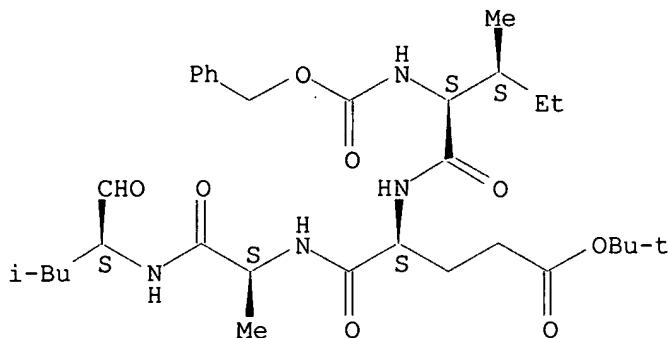
(38) Yasuda, H; Proc Natl Acad Sci USA 1998, V95, P3597 HCPLUS

L59 ANSWER 3 OF 5 HCPLUS COPYRIGHT 2002 ACS
 AN 2000:741943 HCPLUS
 DN 133:291099
 TI Treatment of myeloma bone disease with **proteasomal** and
NF-.kappa.B activity inhibitors
 IN Mundy, Gregory R.
 PA Osteoscreen, Inc., USA
 SO PCT Int. Appl., 22 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K038-04
 ICS A61K031-40; A61K031-166; A61P019-08
 CC 1-6 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000061167	A2	20001019	WO 2000-US9121	20000407
	WO 2000061167	A3	20010111		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1169049	A2	20020109	EP 2000-921764	20000407
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1999-289229	A	19990409		
	WO 2000-US9121	W	20000407		
AB	The present invention involves the identification and use of compns. for treating myeloma bone disease. The compns. inhibit proteasomal activity and decrease the activity of the transcription factor NF-.kappa.B . Assessment of a candidate compd. for its ability to inhibit prodn. or activity of proteasomal enzymes or NF-.kappa.B provides a useful means to identify agents to treat myeloma bone disease.				
ST	bone myeloma therapy proteasome NFkappaB inhibitor; proteasome inhibitor bone myeloma therapy; NF kappaB inhibitor bone myeloma therapy				
IT	Transcription factors RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (NF-.kappa.B (nuclear factor .kappa.B); treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors)				
IT	Antitumor agents (multiple myeloma; treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors)				
IT	5108-96-3 65240-86-0, Ppm-18 158442-41-2 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors)				
IT	140879-24-9, Proteasome RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors)				
IT	158442-41-2 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors)				

RN 158442-41-2 HCAPLUS
 CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 140879-24-9, Proteasome

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (treatment of myeloma bone disease with **proteasomal** and
NF-.kappa.B activity inhibitors)

RN 140879-24-9 HCAPLUS

CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L59 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:478627 HCAPLUS

DN 133:247623

TI Patterns of gene expression associated with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A

AU Ji, Xiaohui; Chen, Di; Xu, Chi; Harris, Steve E.; Mundy, Gregory R.; Yoneda, Toshiyuki

CS Division of Endocrinology and Metabolism, Department of Medicine,
 University of Texas Health Science Center at San Antonio, San Antonio, TX,
 USA

SO J. Bone Miner. Metab. (2000), 18(3), 132-139

CODEN: JBMME4; ISSN: 0914-8779

PB Springer-Verlag Tokyo

DT Journal

LA English

CC 2-10 (Mammalian Hormones)

AB The pluripotent mesenchymal stem cells give rise to osteoblasts, adipocytes, chondrocytes, and myoblasts. The differentiation of these stem cells into each of the mature functional cells may be controlled by a distinctive master gene(s) and is assocd. with temporal and spatial expression of diverse genes. Identification of genes that are expressed during the differentiation of the mesenchymal cells to osteoblasts is, therefore, important to obtain insights into the mol. mechanisms of osteogenesis. The murine undifferentiated mesenchymal cell 3T3-F442A, when treated with the bone morphogenetic protein 2 (BMP-2), a well-characterized inducer of mesenchymal cell differentiation, exhibited both osteoblastic and adipocytic differentiation. Using the SAGE (serial anal. of gene expression) technique, which has been shown to enable quant. anal. of large nos. of genes in a simple and quick manner, the authors obtained 1600 sequence tags representing 2107 individual nucleotide sequences from control and BMP-2-treated 3T3-F442A cells, resp. By comparing the frequency of tag occurrence, the authors found profiles of up- or downregulated genes assocd. with osteoblast or adipocyte phenotype

such as type I collagen, osteonectin and OSF-2, or C/EBP. β ., α P2, fatty acid synthase, and lipoprotein lipase, resp., in BMP-2-treated 3T3-F442A cells. The authors' data show that BMP-2 induces not only osteoblastic but also adipocytic differentiation in the 3T3-F442A cells. They also show that the 3T3-F442A cells have bipotentials of differentiating toward osteoblasts and adipocytes. The results, therefore, might explain the inverse correlation between trabecular bone vol. and fat vol. in the bone marrow cavity. The results also suggest that the SAGE may be a useful technique that allows a fast and efficient way to generate global and local views of gene expression assocd. with cellular differentiation of the mesenchymal stem cells.

- ST BMP2 gene expression osteoblast adipocyte differentiation
- IT Bone morphogenetic proteins
 - RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 - (2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Antigens
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (AD1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Chaperonins
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (ADP ribosylation factor-like protein 2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Transcription factors
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (AP-2 (activator protein 2); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT RNA formation factors
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (C/EBP-. β . (CCAAT box/enhancer element-binding protein . β .); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Transcription factors
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (Cis2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT G proteins (guanine nucleotide-binding proteins)
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (Gs (adenylate cyclase-stimulating), . α .-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Histones
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (H2A; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Heat-shock proteins
 - RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (HSC73; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(J1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L12; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L22; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L32; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L37a; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L5; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(OSF-2 (osteoblast-specific factor-2); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S16; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S2, S28; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S24; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S29; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(TNF-induced protein complex .gamma.; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of

IT mesenchymal progenitor cell 3T3-F442A)
IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal protein P2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal, P1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal, PO; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(adducins, human erythrocyte, .alpha.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Adipose tissue
(adipocyte, differentiation; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Cell differentiation
(adipocyte; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(calcylin; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(calgizzarins; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Chaperonins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(chaperone CCTB; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Osteoblast
(differentiation; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(human ribosomal protein S20; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological

study); FORM (Formation, nonpreparative); PROC (Process)
(human ribosomal protein S7; patterns of gene expression assocd. with
BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal
progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)
(hydrophobic protein MTF; patterns of gene expression assocd. with
BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal
progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)
(insulin-stimulated eIF-4E binding protein; patterns of gene expression
assocd. with BMP-2-induced osteoblast and adipocyte differentiation of
mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)
(jesolin; patterns of gene expression assocd. with BMP-2-induced
osteoblast and adipocyte differentiation of mesenchymal progenitor cell
3T3-F442A)

IT Transcription factors
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)
(junB; patterns of gene expression assocd. with BMP-2-induced
osteoblast and adipocyte differentiation of mesenchymal progenitor cell
3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)
(minopontins; patterns of gene expression assocd. with BMP-2-induced
osteoblast and adipocyte differentiation of mesenchymal progenitor cell
3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)
(mitochondrial ATPase inhibitor; patterns of gene expression assocd.
with BMP-2-induced osteoblast and adipocyte differentiation of
mesenchymal progenitor cell 3T3-F442A)

IT Cell differentiation
(osteoblast; patterns of gene expression assocd. with BMP-2-induced
osteoblast and adipocyte differentiation of mesenchymal progenitor cell
3T3-F442A)

IT Transcription factors
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)
(p68-c-rel; patterns of gene expression assocd. with BMP-2-induced
osteoblast and adipocyte differentiation of mesenchymal progenitor cell
3T3-F442A)

IT Bone formation
(patterns of gene expression assocd. with BMP-2-induced osteoblast and
adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Gene, animal
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(patterns of gene expression assocd. with BMP-2-induced osteoblast and
adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Chloride channel
Fibroblast growth factor receptors
Macrophage migration inhibitory factor
Osteonectin
Ribosomal proteins
Tau factor

- Tubulins
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Proteins, specific or class
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (protein for hereditary multiple exostosis; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Proteins, specific or class
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (rat brain protein; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (rat ribosomal protein L23A; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (rat ribosomal protein S19; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Ribosomal proteins
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (rpA2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Embryo, animal
 (stem cell; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Collagens, biological studies
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (type I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT Anion channel
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (voltage-dependent 3; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT G proteins (guanine nucleotide-binding proteins)
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (.beta.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
- IT **140879-24-9, Proteasome**
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (Rc7-I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 147014-97-9, CDK4 kinase
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (inhibitor; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 9004-02-8, Lipoprotein lipase 9007-43-6, Cytochrome c, biological studies 9036-37-7, Aminolevulinic acid dehydrogenase 9045-77-6, Fatty acid synthase 9059-25-0, Lysyl oxidase 9059-32-9, GTPase 60616-82-2, Cathepsin L
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 9001-16-5, Cytochrome c oxidase
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (subunit VIII; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 37205-63-3, ATP synthase
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (.gamma.-chain precursor and hydrogen-transporting; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 140879-24-9, Proteasome

RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (Rc7-I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell

3T3-F442A)

RN 140879-24-9 HCPLUS
 CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L59 ANSWER 5 OF 5 HCPLUS COPYRIGHT 2002 ACS
 AN 2000:53374 HCPLUS
 DN 132:102860
 TI Inhibitors of proteasomal activity for stimulating bone and hair growth
 IN Mundy, Gregory R.; Garrett, I. Ross; Rossini, G.
 PA Osteoscreen, USA
 SO PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000002548	A2	20000120	WO 1999-US15533	19990709
	W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SD, SG, SI, SK, TR, TT, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9963109	A1	20000201	AU 1999-63109	19990709
	EP 1096924	A1	20010509	EP 1999-933827	19990709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1998-113947 A1 19980710
 WO 1999-US15533 W 19990709

AB Compds. that inhibit the activity of NF-.kappa. B or inhibit the activity of the proteasome or both promote bone formation and hair growth and are thus useful in treating osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation. They also stimulate the prodn. of hair follicles and are thus useful in stimulating hair growth, including hair d., in subject where this is desirable.

ST hair bone growth stimulation NFkappaB inhibitor; proteasome inhibitor hair bone growth stimulation

IT Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (NF-.kappa.B (nuclear factor .kappa.B); NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating bone and hair growth)

IT Bone formation

Drug delivery systems

Drug screening

(NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating bone and hair growth)

IT Bone morphogenetic proteins
 Estrogens

Growth factors, animal
Hormones, animal, biological studies
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-.kappa.B inhibitors and inhibitors of
proteasomal activity for stimulating bone and hair growth, and
use with other agents)

IT Antitumor agents
(bone, metastasis; NF-.kappa.B inhibitors
and inhibitors of proteasomal activity for stimulating bone
and hair growth)

IT Skull
(calvarium, calvarial bone growth assay; NF-.kappa.
B inhibitors and inhibitors of proteasomal activity
for stimulating bone and hair growth)

IT Cartilage
(cartilage-derived morphogenetic proteins; NF-.kappa.
B inhibitors and inhibitors of proteasomal activity
for stimulating bone and hair growth, and use with other agents)

IT Joint, anatomical
(degeneration; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)

IT Disease, animal
(dental; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)

IT Periodontium
(disease; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)

IT Hair
(follicle; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)

IT Bone, disease
(fracture, and bone deficiency; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)

IT Bone
(growth promoters; NF-.kappa.B inhibitors
and inhibitors of proteasomal activity for stimulating bone
and hair growth, and use with other agents)

IT Hair preparations
(growth stimulants; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)

IT Dental materials and appliances
(implants, post-dental implantation; NF-.kappa.
B inhibitors and inhibitors of proteasomal activity
for stimulating bone and hair growth)

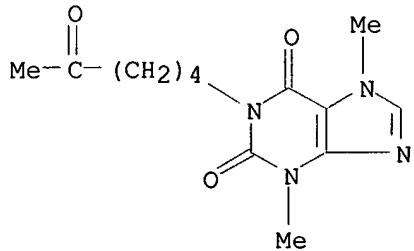
IT Cell differentiation
(inducers; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth, and use with other agents)

IT Bone, neoplasm
(metastasis, inhibitors; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(morphogenetic, cartilage-derived; NF-.kappa.

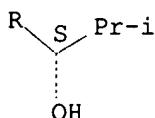
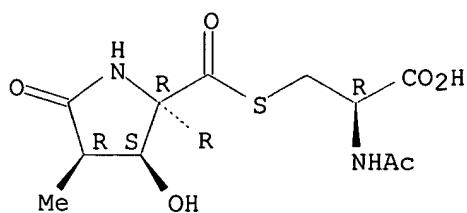
- B inhibitors and inhibitors of proteasomal activity for stimulating bone and hair growth, and use with other agents)**
- IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenins; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth, and use with other agents)
- IT Bone, disease
(osteolytic; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)
- IT Isoprenoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pathway; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)
- IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidic aldehydes; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)
- IT **Aldehydes, biological studies**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidyl; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)
- IT Surgery
(plastic, post-plastic surgery; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)
- IT Joint, anatomical
Prosthetic materials and Prosthetics
(post-prosthetic joint surgery; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)
- IT Hyperparathyroidism
(primary; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)
- IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(proteasome; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)
- IT Bone
(resorption, inhibitors; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth, and use with other agents)
- IT Hyperparathyroidism
(secondary; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)
- IT Osteoporosis
(therapeutic agents; NF-.kappa.B
inhibitors and inhibitors of proteasomal activity for
stimulating bone and hair growth)
- IT Drug delivery systems
(topical; NF-.kappa.B inhibitors and
inhibitors of proteasomal activity for stimulating bone and
hair growth)

- IT 67-99-2, Gliotoxin 404-86-4, Capsaicin 6493-05-6,
 Pentoxifylline 59865-13-3, Cyclosporin A 79902-63-9, Simvastatin
 106096-93-9, Basic fibroblast growth factor 110044-82-1 110115-07-6
133343-34-7, Lactacystin 133407-82-6, MG 132
 133407-86-0, MG 115 158442-41-2 179324-22-2, MG 262
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NF-.kappa.B inhibitors and inhibitors of
 proteasomal activity for stimulating bone and hair growth)
- IT **140879-24-9, Proteasome**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (NF-.kappa.B inhibitors and inhibitors of
 proteasomal activity for stimulating bone and hair growth)
- IT 13598-36-2D, Phosphonic acid, bisphosphonates
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (and statins; NF-.kappa.B inhibitors and
 inhibitors of proteasomal activity for stimulating bone and
 hair growth, and use with other agents)
- IT **6493-05-6, Pentoxifylline 133343-34-7,**
Lactacystin 158442-41-2
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NF-.kappa.B inhibitors and inhibitors of
 proteasomal activity for stimulating bone and hair growth)
- RN 6493-05-6 HCAPLUS
- CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA
 INDEX NAME)



- RN 133343-34-7 HCAPLUS
- CN L-Cysteine, N-acetyl-, (2R,3S,4R)-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA
 INDEX NAME)

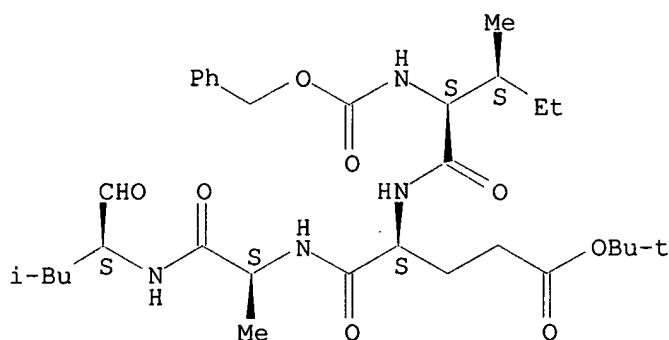
Absolute stereochemistry. Rotation (+).



RN 158442-41-2 HCAPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 140879-24-9, Proteasome

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating bone and hair growth)

RN 140879-24-9 HCAPLUS

CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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FILE 'BIOSIS' ENTERED AT 16:19:56 ON 26 FEB 2002

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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 February 2002 (20020221/ED)

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L193 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:745665 HCPLUS
DN 130:94381
TI **NF-.kappa.B** activation provides the potential link between inflammation and hyperplasia in the **arthritic joint**
AU Miagkov, Alexei V.; Kovalenko, Dmitry V.; Brown, Chadwick E.; Didsbury, John R.; Cogswell, John P.; Stimpson, Stephen A.; Baldwin, Albert S.; Makarov, Sergei S.
CS Thurston Arthritis Research Center, University of North Carolina, Chapel Hill, NC, 27599, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1998), 95(23), 13859-13864
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 15-8 (Immunochemistry)
Section cross-reference(s): 3
AB The transcription factor **NF-.kappa.B** is a pivotal regulator of inflammatory responses. While the activation of **NF-.kappa.B** in the **arthritic joint** has been assocd. with rheumatoid arthritis (RA), its significance is poorly understood. Here, the authors examine the role of **NF-.kappa.B** in animal models of RA. The authors demonstrate that in vitro, **NF-.kappa.B** controlled expression of numerous inflammatory mols. in synoviocytes and protected cells against tumor necrosis factor .alpha. (TNF.alpha.) and Fas ligand (FasL) cytotoxicity. Similar to that obstd. in human RA, **NF-.kappa.B** was activated in the synovium of rats with streptococcal cell wall (SCW)-induced arthritis. In vivo suppression of **NF-.kappa.B** by either proteasomal inhibitors or intraarticular adenoviral gene transfer of super-repressor I.**kappa.B**.alpha. profoundly enhanced apoptosis in the synovium of rats with SCW- and pristane-induced arthritis. This indicated that the activation of **NF-.kappa.B** protected the cells in the synovium against apoptosis and thus provided the potential link between inflammation and hyperplasia. Intraarticular administration of **NF-kB** decoys prevented the recurrence of SCW arthritis in treated joints. Unexpectedly, the severity of arthritis also was inhibited significantly in the contralateral, untreated joints, indicating beneficial systemic effects of local suppression of **NF-.kappa.B**. These results establish a mechanism regulating apoptosis in the **arthritic joint** and indicate the feasibility of therapeutic approaches to RA based on the specific suppression of **NF-.kappa.B**.
ST transcription factor NFkappaB cytokine inflammation hyperplasia rheumatoid arthritis
IT Apoptosis
Rheumatoid arthritis
Synoviocyte
Transcriptional activation
(**NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)
IT **NF-.kappa.B**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)
IT Fas ligand
Interleukin 1.beta.

Interleukin 6

Tumor necrosis factor .alpha.

VCAM-1 (cell adhesion molecule)

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)

(NF-.kappa.B activation in inflamed

synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT **Synovial membrane**

(disease, synovitis; NF-.kappa.

B activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT **Synovial membrane**

(hyperplasia; NF-.kappa.B activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT **Hyperplasia**

(synovial; NF-.kappa.B activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT **Inflammation**

(synovitis; NF-.kappa.B activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (27) van Antwerp, D; Science 1996, V274, P787 HCAPLUS
- (28) Vingsbo, C; Am J Pathol 1996, V149, P1675 HCAPLUS
- (29) Wang, C; Science 1996, V274, P784 HCAPLUS
- (30) Zhou, T; J Immunol 1996, V156, P2661 HCAPLUS
- (31) Zvaifler, N; Am J Pathol 1997, V150, P1125 MEDLINE

L193 ANSWER 2 OF 8 HCPLUS COPYRIGHT 2002 ACS
 AN 1998:263658 HCPLUS
 DN 129:15209
 TI Activation of **NF-.kappa.B** is involved in the survival of **osteoclasts** promoted by interleukin-1
 AU Jimi, Eijiro; Nakamura, Ichiro; Ikebe, Tetsuro; Akiyama, Shuichi; Takahashi, Naoyuki; Suda, Tatsuo
 CS Dep. Biochem., School Dentistry, Showa Univ., Tokyo, 142-8555, Japan
 SO J. Biol. Chem. (1998), 273(15), 8799-8805
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English
 CC 15-5 (Immunochemistry)
 AB The authors previously reported that interleukin-1 (IL-1) promoted the survival of murine **osteoclast-like** cells (OCLs) formed in vitro and activated a transcription factor, **NF-.kappa.B**. The present study examd. whether the activation of **NF-.kappa.B** is directly involved in the survival of OCLs promoted by IL-1. The expression of IL-1 type I receptor mRNA in OCLs was detected by the PCR amplification of reverse-transcribed mRNA. An electrophoretic mobility shift assay showed that IL-1 transiently activated **NF-.kappa.B** in the nuclei of the OCLs, and the maximal activation occurred at 30 min. The degrdn. of **I.kappa.B.alpha.** coincided with the activation of **NF-.kappa.B** in the OCLs. The immunocytochem. study revealed that p65, a subunit of **NF-.kappa.B**, was translocated from the cytoplasm into almost all of the nuclei of the OCLs within 30 min after IL-1 stimulation. The purified OCLs spontaneously died via apoptosis, and IL-1 promoted the survival of OCLs by preventing their apoptosis. The pretreatment of purified OCLs with **proteasome** inhibitors suppressed the IL-1-induced activation of **NF-.kappa.B** and prevented the survival of OCLs supported by IL-1. When OCLs were pretreated with antisense oligodeoxynucleotides to p65 and p50 of **NF-.kappa.B**, the expression of resp. mRNAs by OCLs was suppressed, and the IL-1-induced survival of OCLs was concomitantly inhibited. Thus, IL-1 promotes the survival of **osteoclasts** through the activation of **NF-.kappa.B**.
 ST NF kappaB survival **osteoclast** interleukin 1
 IT Apoptosis
 Osteoclast
 (interleukin-1 promotes **osteoclasts** survival by preventing apoptosis via **NF-.kappa.B** activation)
 IT Interleukin 1
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (interleukin-1 promotes **osteoclasts** survival by preventing apoptosis via **NF-.kappa.B** activation)
 IT **NF-.kappa.B**
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (interleukin-1 promotes **osteoclasts** survival by preventing apoptosis via **NF-.kappa.B** activation)

L193 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
 AN 1997:300447 BIOSIS
 DN PREV199799599650
 TI The **trental** influence on collagen proteolysis in experimental aseptic infarction of the long bone.
 AU Magomedov, S.; Grigorovskii, V. V.
 CS Ukr. Res. Inst. Traumatol. Orthop., Ukr. Minist. Health, Kiev Ukraine

SO Ukrainskii Biokhimicheskii Zhurnal, (1996) Vol. 68, No. 5, pp. 69-76.
 ISSN: 0201-8470.
 DT Article
 LA Russian
 SL Ukrainian; English
 AB Dynamics of biochemical parameters of the connective tissue and morphometric parameters of lesion were studied in rabbits with induced embolic aseptic infarction of the femur without and with the **trental (pentoxyphyllin)** treatment. The correlation was found between the pairs of indices: proteolytic activity and bone marrow necrosis volume; collagenase activity and bone cortex remodelling rate; concentration of protein bound with hydroxyprolin fraction and endosteal regenerate volume.
 CC Biochemical Studies - General *10060
 Cardiovascular System - General; Methods *14501
 Bones, Joints, Fasciae, Connective and Adipose Tissue - General;
 Methods *18001
 Pharmacology - General *22002
 BC Leporidae *86040
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Pharmacology; Skeletal System (Movement and Support)
 IT Chemicals & Biochemicals
 TRENTAL; PENTOXIFYLLINE; COLLAGENASE
 IT Miscellaneous Descriptors
 ASEPTIC INFARCTION; BONE CORTEX REMODELLING RATE; BONE DISEASE; BONE MARROW NECROSIS VOLUME; COLLAGEN PROTEOLYSIS; COLLAGENASE ACTIVITY; ENDOSTEAL REGENERATE VOLUME; EXPERIMENTAL; FEMUR; LONG BONE; PENTOXIFYLLINE; PENTOXYPHYLLIN; PHARMACOLOGY; SKELETAL SYSTEM; TRENTAL INFLUENCE; VASCULAR DISEASE; VASODILATOR-DRUG
 ORGN Super Taxa
 Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 rabbit (Leporidae)
 ORGN Organism Supertaxa
 animals; chordates; lagomorphs; mammals; nonhuman mammals; nonhuman vertebrates; vertebrates
 RN 6493-05-6 (TRENTAL)
 6493-05-6 (PENTOXIFYLLINE)
 9001-12-1 (COLLAGENASE)

L193 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:561734 BIOSIS
 DN PREV200100561734
 TI Regulation of osteoblast differentiation by **proteasome** control of Smad1.
 AU Chen, D. (1); Zhao, M. (1); Qiao, M. (1); Garrett, R. (1); Mi, Z. (1); Crews, C.; Mundy, G. (1)
 CS (1) Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX USA
 SO Journal of Bone and Mineral Research, (September, 2001) Vol. 16, No. Suppl. 1, pp. S145. print.
 Meeting Info.: Twenty-Third Annual Meeting of the American Society for Bone and Mineral Research Phoenix, Arizona, USA October 12-16, 2001
 ISSN: 0884-0431.
 DT Conference
 LA English
 SL English
 CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
 Cytology and Cytochemistry - Animal *02506
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and

BC Biochemistry *18004
 BC Animalia - Unspecified 33000
 IT Major Concepts
 Skeletal System (Movement and Support)
 IT Chemicals & Biochemicals
 Smad-1 protein: osteoblast differentiation regulator,
 proteasome control
 IT Miscellaneous Descriptors
 Meeting Abstract
 ORGN Super Taxa
 Animalia
 ORGN Organism Name
 C2-C12 cell line (Animalia): myoblast-osteoblast precursor cell line,
 osteoblast differentiation
 ORGN Organism Superterms
 Animals

L193 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2000:413041 BIOSIS
 DN PREV200000413041
 TI Specific inhibitors of the chymotryptic component of the
 proteasome are potent bone anabolic agents in vivo.
 AU Garrett, I. R. (1); Gutierrez, G. (1); Chen, D. (1);
 Rossini, G. (1); Escobedo, A. (1); Esparza, J. (1); Horn, D. (1);
 Crews, C. M.; Mundy, G. R. (1)
 CS (1) OsteoScreen, Inc., San Antonio, TX USA
 SO Journal of Bone and Mineral Research, (September, 2000) Vol. 15, No.
 Suppl. 1, pp. S197. print.
 Meeting Info.: Twenty-Second Annual Meeting of the American Society for
 Bone and Mineral Research Toronto, Ontario, Canada September 22-26, 2000
 American Society for Bone and Mineral Research
 . ISSN: 0884-0431.

DT Conference
 LA English
 SL English
 CC Cytology and Cytochemistry - Animal *02506
 Biochemical Studies - General *10060
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and
 Biochemistry *18004
 General Biology - Symposia, Transactions and Proceedings of Conferences,
 Congresses, Review Annals *00520

BC Muridae 86375
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Skeletal System (Movement and
 Support)
 IT Parts, Structures, & Systems of Organisms
 bone: formation, skeletal system; osteoblast: proliferation, skeletal
 system
 IT Chemicals & Biochemicals
 potent bone anabolic agent: in-vivo; specific chymotryptic
 proteasome component inhibitor; statins

IT Miscellaneous Descriptors
 Meeting Abstract
 ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 murine (Muridae)
 ORGN Organism Superterms
 Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
 Rodents; Vertebrates

L193 ANSWER 6 OF 8 MEDLINE
 AN 1998312293 MEDLINE

DN 98312293 PubMed ID: 9648487
 TI Hyperparathyroidism and its management.
 AU Sugimoto T
 CS Department of Medicine, Kobe University School of Medicine.
 SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1998 Jun)
 56 (6) 1591-7. Ref: 36
 Journal code: KIM; 0420546. ISSN: 0047-1852.
 CY Japan
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW LITERATURE)
 LA Japanese
 FS Priority Journals
 EM 199809
 ED Entered STN: 19980917
 Last Updated on STN: 19980917
 Entered Medline: 19980908
 AB Hyperparathyroidism (HPT), resulting from the excess of endogenous parathyroid hormone is cited as one of diseases which cause secondary osteoporosis. HPT consists of primary (1 degree) and secondary (2 degrees) HPT, resulting mainly from chronic renal failure (CRF). HPT is easily distinguishable from primary osteoporosis by biochemical measurements. Parathyroidectomy (PTX) is the only option available for the radical cure of 1 degree HPT and more than 10% increase in bone mass occurs after PTX. On the other hand, dietary phosphorus restriction, phosphorus binders, active vitamin D₃ metabolites are useful for 2 degrees HPT due to CRF. When these treatments are not effective to inhibit PTH secretion adequately, oral active vitamin D₃ pulse therapy, PTX and percutaneous ethanol injection therapy should be considered.
 CT Check Tags: Human
 *Hyperparathyroidism: CO, complications
 *Hyperparathyroidism: TH, therapy
 Hyperparathyroidism, Secondary: CO, complications
 *Osteoporosis: ET, etiology

L193 ANSWER 7 OF 8 MEDLINE
 AN 96302997 MEDLINE
 DN 96302997 PubMed ID: 8741178
 TI Suppressive effect of N-(benzyloxycarbonyl)-L-phenylalanyl-L-tyrosinal on bone resorption in vitro and in vivo.
 AU Woo J T; Yamaguchi K; Hayama T; Kobori T; Sigeizumi S; Sugimoto K; Kondo K; Tsuji T; Ohba Y; Tagami K; Sumitani K
 CS Sagami Chemical Research Center, Kanagawa, Japan.
 SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1996 Apr 4) 300 (1-2) 131-5.
 Journal code: EN6; 1254354. ISSN: 0014-2999.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199610
 ED Entered STN: 19961025
 Last Updated on STN: 19961025
 Entered Medline: 19961017
 AB The suppressive effect of N-(benzyloxycarbonyl)-L-phenylalanyl-L-tyrosinal on bone resorption was examined in vitro and in vivo. This synthetic **peptidyl aldehyde** was found to be a potent and selective cathepsin L inhibitor in our screening for cysteine protease inhibitors. In the pit formation assay with unfractionated rat bone cells, 1.5 nM of this compound markedly inhibited parathyroid hormone-stimulated osteoclastic bone resorption. In addition, intraperitoneal administration of this **peptidyl aldehyde** (2.5-10 mg/kg) for 4 weeks suppressed bone weight loss dose dependently in the ovariectomized mouse,

experimental model of osteoporosis. Hydroxyproline measurement of the decalcified femurs from these ovariectomized mice suggested that this compound acts as a bone resorption suppressor through the inhibition of collagen degradation.

CT Check Tags: Animal; Female; Human
 *Bone Resorption: PP, physiopathology
 *Bone and Bones: DE, drug effects
 Bone and Bones: ME, metabolism
 *Cathepsins: AI, antagonists & inhibitors
 *Cysteine Proteinase Inhibitors: PD, pharmacology
 *Dipeptides: PD, pharmacology
 Leucine: AA, analogs & derivatives
 Leucine: PD, pharmacology
 Mice
 Ovariectomy
 Rats
 Rats, Sprague-Dawley
 RN 66701-25-5 (E 64); 7005-03-0 (Leucine)
 CN 0 (Cysteine Proteinase Inhibitors); 0 (Dipeptides); 0 (N-(benzyloxycarbonyl)-phenylalanyl-tyrosinal); EC 3.4.- (Cathepsins); EC 3.4.22.15 (cathepsin L)

L193 ANSWER 8 OF 8 MEDLINE
 AN 83293098 MEDLINE
 DN 83293098 PubMed ID: 6310016
 TI Studies on osteoporoses. XI. Effects of a methylxanthine derivative. A preliminary report.
 AU Robin J C; Ambrus J L
 SO JOURNAL OF MEDICINE, (1983) 14 (2) 137-45.
 Journal code: IYD; 7505566. ISSN: 0025-7850.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198310
 ED Entered STN: 19900319
 Last Updated on STN: 19900319
 Entered Medline: 19831021
 AB Heparin (500 U/kg s.c. B.I.D.) induced significant osteoporosis in C3H/St(Ha) female mice after 3 months of treatment. **Pentoxifylline** (12 mg/kg i.m. B.I.D.) prevented this experimental osteoporosis. Osteoporosis was measured by in vivo neutron activation analysis and results were confirmed by atomic absorption spectroscopy. **Pentoxifylline** (0.1-100 microgram/ml) increased calcium uptake and cAMP production in osteoblast-like bone cells isolated from fetal Sprague-Dawley rats. Theoretical implications for osteoblast control of bone resorption are discussed.
 CT Check Tags: Animal; Female
 Bone Resorption
 Calcium: ME, metabolism
 Cyclic AMP: ME, metabolism
 Heparin
 Mice
 Mice, Inbred C3H
 Neutron Activation Analysis
 Osteoblasts: DE, drug effects
 Osteoblasts: ME, metabolism
 Osteoporosis: CI, chemically induced
 *Osteoporosis: PC, prevention & control
 *Pentoxifylline: TU, therapeutic use
 Rats
 Rats, Inbred Strains
 Spectrophotometry, Atomic Absorption

Stimulation, Chemical
 *Theobromine: AA, analogs & derivatives
 RN 60-92-4 (Cyclic AMP); 6493-05-6 (Pentoxifylline); 7440-70-2
 (Calcium); 83-67-0 (Theobromine); 9005-49-6 (Heparin)

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 SEE [<<<](http://www.derwent.com/dwpi/updates/dwpicov/index.html)

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L215 ANSWER 1 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2000-686989 [67] WPIX
 DNC C2000-208928
 TI Identifying a compound effective in treating multiple myeloma and myeloma
 bone disease, involves subjecting the compound to an assay determining its
 ability to inhibit NF-kB or proteasomal activity.
 DC B04
 IN MUNDY, G R
 PA (OSTE-N) OSTEOSCREEN INC
 CYC 22
 PI WO 2000061167 A2 20001019 (200067)* EN 22p A61K038-04
 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 W: AU CA JP
 AU 2000042040 A 20001114 (200108) A61K038-04
 EP 1169049 A2 20020109 (200205) EN A61K038-04
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 ADT WO 2000061167 A2 WO 2000-US9121 20000407; AU 2000042040 A AU 2000-42040
 20000407; EP 1169049 A2 EP 2000-921764 20000407, WO 2000-US9121 20000407
 FDT AU 2000042040 A Based on WO 200061167; EP 1169049 A2 Based on WO 200061167
 PRAI US 1999-289229 19990409
 IC ICM A61K038-04
 ICS A61K031-166; A61K031-40; A61P019-08
 AB WO 200061167 A UPAB: 20001223
 NOVELTY - Identifying a compound (I) effective in treating myeloma bone
 disease involves subjecting the compound to an assay to determine its
 ability to inhibit transcription factor NF-kB activity or production, or
 to an assay to determine its ability to inhibit proteasomal enzyme
 activity or production.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:
 (1) a pharmaceutical composition for treating myeloma bone disease
 comprising (I); and
 (2) a method of treating myeloma bone disease by the administration
 of (I).
 ACTIVITY - Osteopathic; cytostatic.

Nine C57BL/KaLwRij mice were inoculated with 0.5 asterisk 106 5TGM-1 cultured myeloma cells and tumor volume was assessed by the formula Tumor volume (cm³) = 4/3((length + width)-1)/2. The mice with tumors were randomized into two groups and treatment was commenced on day 35. One group has **PSI** injected directly into the tumors and the other group has only vehicle injected into the tumors. The tumors in the latter group (untreated mice) continued to grow, resulting in the mice dying between 42 and 55 days after myeloma cell inoculation. The size of the tumors in the treated mice decreased markedly and the mice remained healthy up to 3 months after tumor inoculation, even though treatment was discontinued. The result showed that the treated mice were alive and well with no signs of tumor 4 months after treatment.

MECHANISM OF ACTION - Inhibitor of NF- κ B activity; inhibitor of proteasomal activity.

(I) reduces myeloma tumor volume, delays onset of limb paralysis, decreases the viability of myeloma cells and reduces the volume of tumor marker, IbG2b. (claimed).

USE - (I) is useful for treating multiple myeloma such as osteopenia, osteolytic lesions, osteopetrosis, bone fracture and osteolytic bone disease, and myeloma bone disease (claimed).

Dwg.0/6

FS CPI
FA AB; DCN
MC CPI: B04-C01A; B10-A06; B10-A12A; B14-H01; B14-H01A; B14-L06

L215 ANSWER 2 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-171065 [15] WPIX
DNC C2000-053186
TI Compound that inhibits the activity of NF- κ B useful for enhancing bone formation.
DC B04 B05
IN GARRETT, I R; MUNDY, G R; ROSSINI, G
PA (OSTE-N) OSTEOSCREEN; (OSTE-N) OSTEOSCREEN INC
CYC 73
PI WO 2000002548 A2 20000120 (200015)* EN 37p A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AL AM AU BA BB BG BR CA CN CU CZ EE GE HU IL IN IS JP KP KR LC LK
LR LT LV MD MG MK MN MX NO NZ PL RO SD SG SI SK TR TT US UZ VN
AU 9963109 A 20000201 (200028) A61K031-00
EP 1096924 A1 20010509 (200128) EN A61K031-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000002548 A2 WO 1999-US15533 19990709; AU 9963109 A AU 1999-63109
19990709; EP 1096924 A1 EP 1999-933827 19990709, WO 1999-US15533 19990709
FDT AU 9963109 A Based on WO 200002548; EP 1096924 A1 Based on WO 200002548
PRAI US 1998-113947 19980710
IC ICM A61K031-00
AB WO 200002548 A UPAB: 20000323
NOVELTY - Enhancing bone formation, treating pathological dental conditions, treating degenerative joint conditions by administration of NF- κ B inhibitor.

DETAILED DESCRIPTION - Enhancing bone formation or treating pathological dental conditions or treating degenerative joint conditions in a vertebrate animal comprises administration of a compound that inhibits the activity of NF- κ B or that inhibits **proteasomal** activity or that inhibits production of **proteasome** proteins.

INDEPENDENT CLAIMS are included for the following:

(1) treatment of a condition benefited by stimulating hair growth comprising administration of a compound that inhibits the activity of NF- κ B or that inhibits **proteasomal** activity or that inhibits production of these proteins, and

(2) identifying a compound which enhances bone growth or stimulates hair growth comprising subjecting a candidate compound to an assay to

assess its ability to inhibit:

- (a) NF-kB activity, or
- (b) the production of NF-kB, or
- (c) **proteasomal** activity, or
- (d) the production of enzymes with **proteasomal** activity,

where for all the inhibitory compound is identified as a compound that enhances bone growth.

ACTIVITY - Osteopathic; Endocrine-Gen.; Screening; Vulnerary.

PSI (N-carbobenzoyl-Ile-Glu-(OtBu)-Ala-Leu-CHO) was assayed in vitro for calvarial bone growth. Administered at 0.1, 1 and 5 mg/kg/day, the % increase in bone area compared to control was 21.7, 35.4 and 32.1%, respectively. The 1 and 5 mg/kg/day doses produced an increase in new bone width of 19.9%.

MECHANISM OF ACTION - Antimetastatic; Nuclear-Factor-Inhibitor-Kappa-B.

USE - The method can be used for enhancing bone formation, treating pathological dental conditions, degenerative bone conditions, osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation, and for stimulating hair growth (claimed). The compounds may also be useful in wound healing or tissue repair.

ADVANTAGE - None given.

Dwg.0/1

FS

CPI

FA

AB; DCN

MC

CPI: B04-C01; B06-D13; B06-F05; B07-A02B; B07-D03; B10-A06; B10-A10;
B10-D02; B11-C08; B12-K04A; B14-D03; **B14-N01;**
B14-N06; B14-N11; B14-N17B; **B14-R02**

TECH

UPTX: 20000323

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The compound does not inhibit the isoprenoid pathway. The compound is **lactacystin**, a peptidyl aldehyde or PTX. The method further comprises administration of one or more agents that promote bone growth or that inhibit bone resorption such as bone morphogenetic factors, anti-resorptive agents, osteogenic factors, cartilage-derived morphogenetic proteins, growth hormones, estrogens, bis phosphonates, statins or differentiating factors.